NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE ON AGING

Summary Minutes

The 125th Meeting

NATIONAL ADVISORY COUNCIL ON AGING

May 12–13, 2015

National Institutes of Health
Building 45, P2 Level, Conference Room E1/E2
Bethesda, MD 20892

CONTENTS

Department of Health and Human Services
Public Health Service
National Institutes of Health
National Institute on Aging

NATIONAL ADVISORY COUNCIL ON AGING
SUMMARY MINUTES
May 12–13, 2015

The 125th meeting of the National Advisory Council on Aging (NACA) was convened on Tuesday, May 12, 2015, at 3 p.m. in Building 45, Conference Room E1/E2, National Institutes of Health (NIH), Bethesda, MD. Richard J. Hodes, M.D., Director, National Institute on Aging (NIA), presided.

In accordance with the provisions of Public Law 92–463, the meeting was closed to the public on Tuesday, May 12, from 3 to 5 p.m. for the review, discussion, and evaluation of grant applications in accordance with the provisions set forth in Sections 552(b)(c)(4) and 552(b)(c)(6), Title 5, U.S. Code and Section 10(d) of the Public Law 92–463.[1] The meeting was open to the public on Wednesday, May 13, from 8 a.m. to 1 p.m.

Council Participants:
Dr. Kimberly D. Acquaviva
Dr. Maria C. Carrillo
Dr. Laura L. Carstensen
Dr. Ana M. Cuervo
Dr. Steven R. Cummings
Jennie C. Hansen
Dr. Kevin P. High
Dr. Bradley T. Hyman
Dr. James L. Kirkland
Dr. Eliezer Masliah
Dr. Richard Mayeux
Dr. Charles P. Mouton
Dr. Anne B. Newman
Dr. Thomas A. Rando
Dr. Jonathan S. Skinner

Absent Council Members
Dr. Reisa A. Sperling
Dr. Debra Bailey Whitman

[1] For the record, it is noted that members absented themselves from the meeting when the Council discussed applications (a) from their respective institutions or (b) in which a conflict of interest may have occurred. This procedure only applied to applications that were discussed individually, not to "en bloc" actions.

Ex Officio Participants:
Dr. Richard M. Allman, Veterans Health Administration
Dr. Jane Tilly, Administration for Community Living

Absent Ex Officio Participants:
Dr. Kenneth G. Pugh, National Naval Medical Center
Edwin L. Walker, Administration on Aging

The Council Roster, which gives titles, affiliations, and terms of appointment, is appended to these minutes as attachment A.

In Addition to NIA Staff, Other Federal Employees Present:
Dr. Anne Batam, Center for Scientific Review (CSR), NIH
Dr. Valerie Durrant, CSR, NIH
Dr. Samuel Edwards, CSR, NIH
Dr. Alexei Kondratyev, CSR, NIH

Members of the Public Present:
Dr. Elissa S. Epel, University of California, San Francisco
Dr. J. Taylor Harden, National Hartford Centers of Gerontological Nursing Excellence
Dr. Rose Maria Li, Rose Li and Associates, Inc.
Dr. Frances McFarland Horne, Rose Li and Associates, Inc.

I. REVIEW OF APPLICATIONS

This portion of the meeting was closed to the public, in accordance with the determination that it concerned matters exempt from mandatory disclosure under Sections 552(b)(c)(4) and 552(b)(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix).[2]

A total of 2838 applications requesting $4,694,179,967 for all years underwent initial review. The Council recommended 1631 awards for a total of $2,978,086,567 for all years. The actual funding of the awards recommended is determined by the availability of funds, percentile ranks, priority scores, and program relevance.

II. CALL TO ORDER

Dr. Hodes welcomed members to the open session of the 125th NACA meeting and called the meeting to order at 8 a.m. on Wednesday, May 13, 2015.

A. Director's Status Report

Dr. Hodes began his report by recognizing Richard Suzman, Ph.D., director of the Division of Behavioral and Social Research (DBSR), who passed away on April 16,

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2015. Dr. Hodes noted the many articles that captured Dr. Suzman's unique contributions and he commended the DBSR staff for maintaining Division operations while grieving. John Haaga, Ph.D., is serving as acting director for the Division and a search for a new director is under way.

In his budget update, Dr. Hodes reminded the Council that the budgets for NIH and NIA remain flat and have not recovered to pre-sequestration levels. Despite increases since the sequestration, annual budgets declined in purchasing power since 2005. In fiscal years 2013 and 2014, the percentage increase allocated to NIA was higher than that allocated to NIH overall, but the bulk of that increase reflects a substantial increase in research dollars for Alzheimer's Disease (AD).

As the table below shows, the general payline was low this year and much lower than the payline of Alzheimer's research. Dr. Hodes said that the lower general payline resulted from both an increase in the number of applications received by NIA and an increase in the number of NIA applications that fared well in review.

	<500 K		>500 K	
	General	AD	General	AD
Payline	8	14	5	11
New Investigators (R01)	12	18	9	15
Early Stage Investigators (R01)	14	20	11	17

Dr. Hodes reminded the Council that language in the 2015 appropriations legislation requires NIH to submit an annual bypass budget for AD research. In this budget, NIH will state the resources needed to achieve the milestones detailed in The National Plan to Address Alzheimer's Disease. With a large amount of scientific input, NIH led the development of specific milestones and related goals, objectives, and priorities. Currently, NIH is developing budget estimates and plans to submit the AD bypass budget for review by the HHS secretary in July. Although the HHS secretary and the Advisory Council on Alzheimer's Research, Care, and Services will have opportunities to review and comment on the budget, they cannot alter it.

Dr. Hodes also reported that the NCATS Repurposing Program, which supports a range of activities to make FDA-approved drugs available for new uses, has generated preliminary data suggesting that an approved cancer therapy may also benefit AD. NIA was involved in this research. Dr. Hodes also noted the President's Precision Medicine Initiative, which will apply sequencing and other information to precision medicine for cancer in the near term and generate a knowledge base to move precision medicine into all areas of health and disease in the long term. Part of this initiative will involve developing a national cohort of 1 million participants, along with a database and

repository containing genomic data, lifestyle information, and biologic samples linked to electronic health records.

Dr. Hodes closed his report by highlighting the AD Summit, which was held on February 9–10, 2015. Several overarching themes emerged from this Summit:

- Understanding all aspects of healthy brain aging and cognitive resilience to inform strategies for AD prevention
- Integrative, data-driven research approaches such as systems biology and systems pharmacology
- Computational tools and infrastructure
- Leveraging use of wearable sensors and other mobile health technologies to analyze behaviors related to dementia progression
- Enabling open science in basic, translational, and clinical research
- Changing academic, publishing, and funding incentives to promote collaboration, transparency, and reproducible research
- Investing in the development of a new translational and data science workforce
- Engaging citizens, caregivers, and patients as equal partners in AD research

Summit recommendations have been finalized and will be presented to Council at a later date.

In response to questions from James Kirkland, Ph.D., Dr. Hodes noted the difficulty in predicting future paylines. He acknowledged concerns, among the scientific community, regarding smaller, investigator-initiated research projects, and he concurred with Dr. Kirkland's comment that many of the greatest scientific advances have emerged from such projects. Dr. Hodes reminded the Council that NIA seeks to balance funding for smaller projects with larger, more expensive ones, while considering the need for new programs, such as those for new and early-stage investigators and differential paylines for various mechanisms.

The Council also discussed 21st Century Cures, a Congressional initiative to accelerate the process of treatment discovery, development, and delivery.

B. Future Meeting Dates

September 16-17, 2015 (Wednesday and Thursday, Building 31)
January 19–20, 2016 (Tuesday and Wednesday, Building 31)
May 10–11, 2016 (Tuesday and Wednesday, Building 31)
September 27–28 (Tuesday and Wednesday, Building 31)

C. Consideration of Minutes of the Last Meeting

The minutes of the January 2015 meeting were considered. A motion was made, seconded, and passed unanimously to approve the minutes.

III. REPORT: TASK FORCE ON MINORITY AGING RESEARCH

Charles Mouton, M.D., summarized two presentations given to the Task Force during the previous day's meeting. The first, by Kenneth Gibbs, Ph.D., described work exploring career interests and training experiences among recent Ph.D. graduates in science, technology, engineering, and mathematics. Through focus groups, a national survey, and in-depth interviews, Dr. Gibbs and his colleagues received 1,500 responses representing 5% of all American biomedical Ph.D. graduates and 10% of those from underrepresented minority groups. Responses indicated an overall decline in interest in faculty research careers, particularly among individuals at research-intensive institutions and particularly among underrepresented minority populations. Men cited low postdoctoral pay and difficulties in the job market and grant environment as reasons for their loss of interest, whereas women more often cited life balance and the general research climate as reasons. Despite similarities in initial interest, productivity, advisory investment, and research self-sufficiency, responses also showed disparate interest in Ph.D. completion. Dr. Gibbs and his colleagues concluded that interest in research careers was shaped both by personal values and structural dynamics and that new or revised institutional-level policies are needed to address these concerns. The second talk, given by Janet Paluh, Ph.D., focused on pluripotency and ethnic diversity in neural and cardiac stem cell tissue engineering. Dr. Paluh discussed a cluster analysis of stem cells, using international reference genotypes obtained primarily from samples of Northern European, Western European, and Middle Eastern origin. Ultimately, the analysis demonstrated how stem cells may contribute to health disparities. Dr. Paluh described the need to follow stem cells and gene expression over longer periods of time and how nanotechnology can be used to better understand such topics as neural connectivity. Following this presentation, the Task Force discussed within-group diversity in self-reported race and ethnicity, how specific single nucleotide polymorphisms in pluripotent cells might indicate differential disease expression, and the need to include a broader base of team members to enhance collaborative research.

Dr. Mouton concluded his report by noting a concept clearance reviewed by the Task Force: Aging Research on Stress and Resilience to Address Health Disparities in the United States. This concept was described further during the report from the Working Group on Program.

IV. REPORT: COUNCIL OF COUNCILS

Ana M. Cuervo. Ph.D., reported on the January 2015 meeting of the Council of Councils (CoC), which took place after the January NACA meeting. One discussion item at this meeting involved centralized non-human primate (NHP) resources supported by the Office of Research Infrastructure Programs. The Primate Centers provide infrastructure,

animals, and expertise; collaborate with NIH-funded grantees; and provide a home base for researchers conducting cutting-edge science involving NHPs. The program, funded at $94 million, comprises seven large centers, six specialized centers, and specific pathogen-free colonies, employing 300 core scientists and 2,000 affiliates. Rhesus macaques represent 60% of the total NHP population at these centers. The program has supported approximately 1,000 individual projects, 30% of which focus on HIV/AIDS. Dr. Cuervo also noted that the Simian Immunodeficiency Virus could not be used as a model to produce potential AIDS vaccines had NHPs not been available. .

The CoC also heard an update from Lawrence Tabak, Ph.D., principal deputy director of NIH, who discussed support for biomedical research, the biomedical research workforce, and exceptional opportunities such as the NIH BRAIN Initiative, Ebola research, and precision medicine. Dr. Cuervo highlighted Dr. Tabak's comments concerning international changes in the biomedical workforce. For example, Dr. Tabak noted that while the U.S. biomedical workforce continues to grow, the biomedical workforce in countries such as China is growing more rapidly. In the past, China and other countries have provided many U.S. trainees. Dr. Tabak noted that the United States might not continue to have the luxury of recruiting its workforce from other countries and emphasized the need to engage more American individuals in science.

Dr. Cuervo also reported on recent activities related to the NIH Common Fund. She highlighted a task force established by the CoC to evaluate the principles and procedures in Common Fund management, assess the impact of science supported by the Common Fund, and provide recommendations to optimize the success and impact of the Common Fund. The task force has generated 47 recommendations. Dr. Cuervo highlighted some of these recommendations:

Strategic Planning

- Engage a broad group of stakeholders to gather and shape ideas.
- Clarify criteria for new Common Fund programs.
- Engage Institute and Center (IC) directors and identify potential skeptics of specific proposals.

Program Management

- Increase communication and publicity.
- Ensure evaluation plans are developed early in the program life-cycle.
- Familiarize everyone with the Common Fund process.
- Establish kickoff and annual grantee meetings.
- Include an evaluation at the midpoint of the funding term.

In response to this evaluation, the CoC now provides a second level of review to all applications for high-risk, high-reward initiatives, not just the Early Independence and

Transformative Research Awards. That means that the CoC also provides second-level review for the Pioneer and New Innovator Awards. In addition, the concept clearance process has changed such that a small group of IC directors vet concepts before the CoC reviews the proposals. This allows the IC directors to give more targeted input and for clearer concepts to be presented to the CoC. Although these changes have reduced the number of concepts seen by the CoC, the concepts are better developed, allowing for richer input from the Council. In response to questions from Richard Mayeux, M.D., about the general decline in the number of individuals entering the biomedical workforce, Dr. Cuervo noted that the issues presented to the Task Force on Minority Aging Research in Dr. Gibb's presentation highlighting decline in interest on faculty positions for URM were applicable in general. However, the CoC did not discuss issues with recruitment and retention. In response to questions from Eliezer Masliah, M.D., regarding the future of NHP centers, Dr. Cuervo pointed out that centralized NHP centers were created because NIH remains aware of the unique contribution of such research. She noted the need to ensure access to these centers and increase publicity to increase awareness.

V. NACA PHYSICIAN-SCIENTIST WORKING GROUP

Although the number of K award applications from Ph.D.s has increased by approximately 50%, the number of applications from M.D.s and M.D./Ph.D.s has decreased. Kevin High, M.D., Chair of the Working Group updated the Council on the activities of a working group assessing reasons for decline.

The Working Group met with Dr. Sherry Mills, Director NIH Office of Science Policy and co-chair of the NIH Physician-Scientist Working Committee and discussed NIA Physician Scientist Awards. The NACA Physician-Scientist Working Group found the number of applications from physician-scientists, particularly for K08 awards, has declined from 50% of all K applications in 2002–2003 to 5% in 2012. The major reasons for this decline include uncertainty about grant-funded research careers for young physician-scientists, salaries outpacing K awards, the decreased ability of departments and institutions to fill pay gaps, and the inability to fulfill the requirement for 25% protected time. The data suggest that during the past 5 years, only half of physician-scientists receiving an R01 had a K award first. However, the average amount of time from degree to the first R01 is on average 2 years shorter with the K award than without it. Therefore, the NACA working group concludes that the K award is a strong mechanism that is underused.

Dr. High highlighted the working group's recommendations for physician-scientists:

- Increase the dollar amount for each K award, commensurate with covering the same percentage of salary in 2015 as was covered when the award program was first established.
- Establish a "step-down" K award that would allow less than a 75% effort and allow physician-scientists to receive concomitant funding from other sources.

- Foster creative ways to continue K research mechanisms, such as the K99/R00, and make them friendlier toward physician-scientists.
- Continue expanding related mechanisms such as the Grants for Early Medical/Surgical Specialists Transition to Aging Research (GEMSSTAR) and the Paul B. Beeson Career Development Awards in Aging Research.
- Implement periodic reporting to NACA on these funding mechanisms and their success.

The NACA working group is refining its report based on feedback from junior and senior faculty. The final recommendations will be presented at the September NACA meeting.

VI. PRELIMINARY REPORT: DGCG REVIEW

Dr. High reported on a meeting of the working group tasked with reviewing the Division of Geriatrics and Clinical Gerontology (DGCG). The reports under development by the working group emphasize five general themes:

- Translation. The Division's efforts toward translation should be accelerated as much as possible and collaboration across NIA Divisions should be promoted. A meeting of directors from NIA-supported centers and the development of a phenotypic dataset were specific suggestions under this theme.
- Training. Several programs, such as the GEMSSTAR and Beeson awards, have been highly successful, not only because of the money they have granted but also because of the communities they have helped to establish. The working group suggested expanding T35 and M.D./Ph.D.-focused award mechanisms.
- Leveraging partners by developing knitted cohorts. The working group suggests building a network that emphasizes clinical research. Such a network could include international partners and be modeled after the NIH Geroscience Group.
- Developing additional strengths in new research paradigms. These efforts include focusing on other –omics, such as epigenomics and metabolomics; the growing partnership with the Patient-Centered Outcomes Research Institute; and increasing research based on big data and electronic medical records.
- Review. As is the case for all applications in aging research, applications for DGCG address complex research questions and are a poor fit for traditional study sections, which focus on reductionist approaches. This is a particular problem for expensive clinical studies.

VII. REPORT: WORKING GROUP ON PROGRAM

The Working Group on Program considered one report and two concept clearances.

A. Recommendations from Past Meetings

Dr. High briefly noted the final report from the meeting on the NIA Clinical Trials Advisory Panel. He then reported that the Working Group on Program has forwarded a motion to accept recommendations generated by the AD Summit. There were no amendments to the recommendations. The motion to accept the recommendations was seconded and passed unanimously by the Council.

B. RFA/RFP Concept Clearances

Look AHEAD

The Look AHEAD study is a successful, randomized, controlled trial of intensive lifestyle modifications for the treatment of diabetes. The study now has an opportunity to add aging-related measures such as walking speed and functional performance. NIA is requesting approval to co-fund the aging-related components as other ICs sustain and continue Look AHEAD. The Working Group agreed that this was an enormous opportunity for aging research, in line with its recommendations to incorporate aging research components into trials supported by other ICs. Working Group members also believed that this is an exciting opportunity to understand how diabetes influences aging. The Working Group forwarded the motion that this request be approved. In response to questions from the Council, the Working Group confirmed that these components include measures of cognition. The motion to approve the request was seconded and passed unanimously by the Council.

Aging Research on Stress and Resilience to Address Health Disparities in the United States.

This initiative was developed in response to a review by the Task Force on Minority Aging Research and the finding of gaps in research related to aging-related health disparities. In 2014, the Council approved a framework to prioritize research to address health disparities in aging research and this initiative was designed to address a cross-cutting theme—stress and resilience—that appeared in this framework. The initiative will require specialized expertise and interdisciplinary collaboration, particularly in peer review. It also represents an opportunity for collaboration across the four NIA Divisions. The Working Group enthusiastically motioned that this initiative be approved. The motion was seconded and passed unanimously by the Council.

C. Statement of Understanding

Robin Barr, D. Phil., reminded the Council that the Statement of Understanding is an agreement between NACA and NIA staff on routine business, such as small supplements or reinstatements, which can be done without Council action. A motion to renew the Statement of Understanding, with a modification removing a sentence regarding the reinstatement of funds to a grant application, was forwarded and seconded. The motion passed unanimously.

D. Statistical Package

Dr. Barr noted two tables reflecting the number of applications received for this round and how well they fared in review.

VIII. PROGRAM HIGHLIGHTS

A. Division of Neuroscience (DN): Alpha-Synuclein as an Immunotherapy Target for AD and Synucleinopathies of the Aging

Dr. Eliezer Masliah, a new Council member, described his work exploring ways to manipulate α-synuclein to treat various aging associated neurodegenerative disorders. α-synuclein is a highly abundant amino acid molecule found in pre-synaptic terminals and plays a role in synaptic function and neurotransmission. Although initially cloned from patients with AD, it has since been associated with several other aging-associated neurodegenerative disorders. α-synuclein plays a role in accumulating proteins that damage synapses and interacts with other pathogenic proteins such as ApoE4, amyloid beta (Aβ), and tau. Approximately 75% of patients with AD display accumulations of α-synuclein in areas of the limbic system, including the amygdala. As with Aβ or tau, α-synuclein appears to drive pathogenesis by forming smaller molecular complexes, or oligomers, that lodge in neural membranes and propagate across neurons. Thus, α-synuclein may be an important therapeutic target in AD and other neurodegenerative disorders.

Dr. Masliah and his colleagues have shown that actively immunizing both younger and older transgenic mice, using CFA + α-synuclein decreases the pathogenic accumulation of α-synuclein and synaptic pathology while increasing lysosomal activity. Because of accumulating evidence that active immunization with antigens maybe problematic, the researchers also collaborated with a company to identify "Affitopes®" that mimic the immunogenicity of α-synuclein without eliciting autoimmune or nonspecific reactions. In doing so, they demonstrated that antibodies generated against these Affitopes® reduce α-synuclein accumulation and behavioral deficits in both young and aged mice. Further work showed that immunization targeting α-synuclein Affitopes® protects against the degeneration of choline and dopamine seen in mouse models that are transgenic for both α-synuclein accumulation and AD. The researchers also found that immunization targeting Aβ Affitopes® offers glutaminergic protection. These results indicate that Aβ and α-synuclein target different populations of neurons and might be modulated with different types of vaccines.

Dr. Masliah and his colleagues also have explored the use of passive immunization to target propagating α-synuclein. They found that transplanting neuronal stem cells protects against α-synuclein accumulation, as does injecting antibodies targeting various domains of α-synuclein. In addition, Dr. Masliah's group demonstrated that single-chain antibodies against oligomers of α-synuclein and ApoB traffic at higher levels into the central nervous system, recognize propagating α-synuclein, and clear it via autophagy. Clinical trials of both active and passive immunization are under way.

Discussion focused on opportunities for collaboration and on ways to adapt Dr. Masliah's assays for use in human studies.

B. Division of Geriatrics and Clinical Gerontology (DGCG): Epidemiologic Insights into Human Aging

Dr. Anne Newman a new Council member described the work of her and her colleagues towards developing a physiological index of morbidity. Aging can be defined as an accumulation of damage and repair in cells, tissues, organs, and a person over time. This accumulation is universal, detrimental, and inevitable, resulting in loss of function and in vulnerability to disease. Traditional epidemiologic models have viewed disease as selective and preventable and focused on identifying modifiable targets. However, recent research on various biologic mechanisms has begun to identify an aging phenotype and develop a model with modifiable risk factors that may influence disability and vulnerability. By looking across specific causes of death, Anne Newman. M.D., and her colleagues have identified a pattern suggesting that organ systems vary in susceptibility to damage, with age. For example, cancer deaths occur earlier than cardiovascular deaths, which in turn occur earlier than dementia-associated deaths. This pattern persists even after controlling for external factors. Dr. Newman and her colleagues have used this pattern to categorize risk factors but found that age remains a strong, independent risk factor for mortality and disability.

To identify patterns and characteristics associated with longevity, Dr. Newman and her colleagues have focused on a cohort of 2,000 individuals from the Cardiovascular Health Study who lived to be 90 years or older. Although the observations suggest that human aging involves a collection of independent systems, the researchers have developed a physiologic index of comorbidity that can identify the small cohort of exceptionally healthy individuals. This index explained about 40% of age-associated mortality. To accommodate other population studies with less detailed phenotyping, Dr. Newman and colleagues have developed a healthy aging index that substitutes measures more readily available worldwide. This index allows them to assess the heritability of, and potential genetic loci associated with longer life. Both indexes link intrinsic factors and biomarkers to function, longevity, and healthy aging among unique populations.

Dr. Newman and her colleagues are conducting a meta-analysis of 19,500 study participants from the Cohorts for Heart and Aging Research in Genomic Epidemiology consortium. The researchers are using their healthy aging index to assess frailty and model trajectories of age-associated decline.

Discussion focused on the technical aspects of Dr. Newman's work and the applicability of the healthy aging index to animal models.

C. Division of Aging Biology (DAB): The Epigenetics of Aging: In Search of a Definition of Cellular Age

Thomas Rando, Ph.D., Council member, discussed epigenetics and how to manipulate it with respect to tissue repair, particularly in skeletal muscle. Epigenetics is the study of cellular and physiologic trait variations that are not caused by changes in DNA sequence. Epigenetic changes are apparent, for example, in the vast differences

between cell types despite them sharing the same DNA. Induced pluripotent cells, which are generated by exposing differentiated cells to factors that revert them to their pluripotent state, and fertilized eggs are other examples of epigenetic influences.

Fetuses and newborns display a remarkable regenerative capacity. Following injury, stem cells activate and proliferate, eventually differentiating into new muscle cells. This regenerative potential declines with age, partly as a result of declining function in stem cells and aged tissues. This is illustrated in mice, which show less regeneration and more scarring with older age. One study showed that when a molecule that activates the Notch signaling pathway is administered simultaneously with a small injury to muscle in an older mouse, the mouse displays a regenerative capacity similar to that seen in younger mice. This reversibility has also been shown in parabiosis experiments, in which two mice share a circulatory system. When an older mouse is paired with a younger one (heterochronic pairing), tissue repairs just as well in the older mouse as in the younger one. Similar results are seen when plasma from younger mice is transferred to older ones and in different tissues from the skin, liver, and brain. These findings suggest the presence of circulating factors that influence stem cells, and several of those factors have been identified. Dr. Rando also discussed how the events that occur at fertilization could be viewed as a form of epigenetic rejuvenation and whether there is an epigenetic signature that can reveal cellular age at the molecular level. To examine such an epigenetic signature and determine whether older cells can be epigenetically reprogrammed to a younger state, Dr. Rando and his colleagues conducted a transcriptional analysis of younger and older muscle stem cells. This analysis showed an axis of aging, with expression patterns of stem cells from heterochronic pairing falling in between those of older and younger cells. Cells from older and younger mice also showed differences in histone modifications. For example, with increasing age, differences appeared in the methylation of lysine 27 on histone 3 (H3K27me3) and in DNA methylation across the genome. With heterochronic parabiosis, older cells appeared to revert to a youthful phenotype. A clearer understanding of age-associated epigenetic states may provide insight into ways to repair muscles as they age or after injury. Dr. Rando and his colleagues also are investigating the relationship between circulatory factors that affect cell age and the health benefits of exercise. Work is under way in both mice and humans. For example, Dr. Rando's group has found that exercise induced neurogenesis in mice and they are studying the effects of neurogenesis-associated factors when introduced into older mice. Learning, memory, and behavioral tests are also under study.

Council discussion focused on the technical aspects of Dr. Rando's work.

D. Division of Behavioral and Social Research (DBSR): Psychological Stress, Physiological Stress, and Cellular Aging Mechanisms

Elissa Epel, Ph.D., of the University of California—San Francisco, described her work exploring the risk between psychological stress and cellular aging, The model of allostatic load explains how the slow wear and tear of aging has a cumulative toll on regulatory systems, leading to damage. Traditionally, these phenomena have been

measured as risk factors such as metabolic syndrome and stress hormone levels. However, measurement of cellular aging, which is the building block of tissue aging, may provide a more sensitive way to monitor the effects of allostatic load. Dr. Epel has focused on the telomere, a repeating DNA sequence at the ends of chromosomes. It is not fully replicated as cells divide because of the limitations of DNA polymerases and when the telomere becomes too short, the cell can become senescent and pro-inflammatory. Telomerase, which contains both a protein component and a reverse transcriptase component, adds back nucleotides to promote and rebuild the telomere. Increasing evidence suggests that telomerase is particularly sensitive to daily stress.

In a study comparing young, healthy mothers caring for children with special needs (high-stress mothers) with low-stress mothers, Dr. Epel and her colleagues found that high stress is associated with significantly shorter telomeres and higher levels of oxidative stress. This finding is consistent with several other population studies associating telomere shortening with caregiving, trauma, anxiety, lower education level, poor diet, and metal exposures. The findings also are consistent with animal studies, particularly in birds, showing associations among social isolation, telomere shortening, and mortality. In a cohort of 5,000 participants from the Health and Retirement Study, Dr. Epel and her colleagues found that the extent of childhood adversity is a strong, independent predictor of the extent of telomere shortening in older adults.

Dr. Epel and her colleagues are looking further at cellular phenotypes associated with stress. They found that chronic stress mimics chronologic age with respect to telomerase activity, particularly in CD28-negative lymphocytes, which display a senescent and pro-inflammatory phenotype. They also assessed mitochondrial health, which is driven in part by telomeres, and found that mitochondrial health is worse in high-stress women than in low-stress women with similar numbers of mitochondria. In addition, Dr. Epel and her colleagues have found that higher stress is associated with an accelerated decline in klotho, a hormone that is associated with longevity and better functioning and cognition and that normally declines with age. These studies provide cellular and molecular evidence that stress accelerates aging.

Dr. Epel closed her presentation by describing work suggesting that chronic stress, such as that associated with caregiving, is a syndrome that involves hyper-responsiveness to daily stress. She also noted ongoing work to develop validated measures of stress and partnerships with global, NIA-supported studies of aging. She pointed to cellular resistance to stress as an exciting model in aging biology, with significant opportunities for research using animal and human models. She also noted potential for future research in translational geroscience.

The Council discussed the technical aspects of Dr. Epel's work and distinctions between threat and challenge stress.

IX. ADJOURNMENT

The open session of the 125th meeting of the National Advisory Council on Aging adjourned at 12:40 p.m. on May 13, 2015. The next meeting is scheduled for September 16–17, 2015.

X. CERTIFICATION

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.[3]

Richard J. Hodes

Richard J. Hodes, M.D.
Chairman, National Advisory Council on Aging
Director, National Institute on Aging

Prepared by Robin Barr, D. Phil
With assistance by Rose Li and Associates, Inc.

[3] These minutes will be approved formally by Council at the next meeting on September 16–17, 2015, and corrections or notations will be stated in the minutes of that meeting.

NATIONAL INSTITUTE ON AGING

DIRECTOR'S STATUS REPORT JANUARY 2015

Dr. Richard Hodes, Director (NIH/NIA) [E]

05/13/2015

DIRECTOR'S STATUS REPORT
National Institute on Aging
MAY 2015

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BUDGET and APPROPRIATIONS

Status of FY 2015, 2016, and 2017 Budgets

FY 2015

The President signed into law a $1.1 trillion Omnibus spending bill on December 16, 2014 to keep most of the federal government funded through September 2015. For NIA, the FY 2015 level was $1,199.468 million. An amount of $1.945 million was transferred to the NIH Office of AIDS Research for HIV/AIDS, resulting in a revised operating level of $1,197.523 million. This amount includes $25 million for Alzheimer's Disease funding. The operating budget allows for 1,424 total research project grants (RPGs), including 380 new and competing awards. The estimate includes $98.244 million for research centers, $40.378 million for other research, and $25.150 million for research training. The R&D contract mechanism will be supported at a level of $57.200 million.

FY 2016

The FY 2016 President's budget was released to the public on February 2, 2015. The President's request for NIH is $31.311 billion, which is $1 billion higher than the FY 2015 level of $30.311 billion.

The NIA budget request for FY 2016 is $1,267.078 million, an increase of $69.555 million over the FY 2015 comparable enacted level. This amount includes $50 million for Alzheimer's Disease funding. The NIA FY 2016 Congressional Justification can be viewed at http://www.nia.nih.gov/about/budget/2015/fiscal-year-2016-budget.

For NIA, the FY 2016 President's Budget will allow for 1,538 total research project grants (RPGs), including 403 new and competing awards. The estimate includes $103.196 million for research centers, $40.378 million for other research grants, and $25.150 million for research training. The R&D contract mechanism will be supported at a level of $65.311 million.

FY 2017

Preliminary work on the budget for FY 2017 has begun using the FY 2016 President's budget request as the base. After intermediate stages of review, the President's budget request for FY 2017 will be presented to Congress in February 2016, at which time it will become available to the public.

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

(Dollars in thousands)

MECHANISM	FY 2014 Final Allocation		1/ FY 2015 Operating Plan		2/ FY 2016 President's Budget	
Research Grants	No.	Amount	No.	Amount	No.	Amount
Research Projects						
Noncompeting	958	492,293	958	496,721	1,040	539,411
Administrative Supplements	(106)	10,438	(107)	10,500	(107)	10,500
Competing	385	260,875	380	266,864	403	275,567
Subtotal	1,343	763,606	1,338	774,085	1,443	825,478
SBIR/STTR	80	32,084	86	34,650	95	38,071
Subtotal, RPG	1,423	795,690	1,424	808,735	1,538	863,549
Research Centers						
Specialized/Comprehensive	78	90,653	84	97,098	88	102,050
Clinical Research	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0
Comparative Medicine	0	1,146	0	1,146	0	1,146
Res. Centers in Minority Instit.	0	0	0	0	0	0
Subtotal, Centers	78	91,799	84	98,244	88	103,196
Other Research						
Research Careers	199	27,355	203	27,960	203	27,960
Cancer Education	0	0	0	0	0	0
Cooperative Clinical Research	0	0	0	0	0	0
Biomedical Research Support	0	0	0	0	0	0
Minority Biomed. Res. Support	0	0	0	0	0	0
Other	52	12,157	53	12,418	53	12,418
Subtotal, Other Research	251	39,512	256	40,378	256	40,378
Total Research Grants	1,752	927,001	1,764	947,357	1,882	1,007,123
Training	FTTP		FTTP		FTTP	
Individual	150	6,430	150	6,924	148	6,924
Institutional	388	17,176	388	18,226	384	18,226
Total Training	538	23,606	538	25,150	532	25,150
Research & Develop. Contracts	81	59,113	78	57,200	78	65,311
(SBIR/STTR)	(4)	(349)	(4)	(360)	(4)	(360)
Intramural Research		118,794		123,316		124,549
Res. Management & Support		43,203		44,500		44,945
Total, NIA		1,171,717		1,197,523		1,267,078

1/ FY 2015 includes $25 million for Alzheimer's Disease
2/ FY 2016 includes $50 million for Alzheimer's Disease

LEGISLATIVE UPDATE

May 2015

Proposed Legislation of Interest to the NIA/NIH:

S. 289 – On January 28, 2015, Senator Richard Durbin (D-IL) introduced S. 289, the American Cures Act. The bill would authorize additional investment for NIH, CDC, Department of Defense Health Program, and Veterans Medical & Prosthetics Research Program and also create a budget cap adjustment through the remaining years of the Budget Control Act. S. 289 was referred to the Senate Committee on the Budget.

S. 318/H.R. 531 – On January 29, 2015, and January 26, 2015, Senator Barbara Mikulski (D-MD) and Representative Rosa DeLauro (D-CT) introduced S. 318 and H.R. 531, respectively, the Accelerating Biomedical Research Act. These bills would prioritize funding for the National Institutes of Health to discover treatments and cures, to maintain global leadership in medical innovation, and to restore the purchasing power the NIH had after the historic doubling campaign that ended in fiscal year 2003. Senator Benjamin Cardin (D-MD) co-sponsored S. 318 and Representatives Brian Higgins (D-NY) and Peter King (R-NY) co-sponsored H.R. 531. S. 318 and H.R. 531 were referred to Senate and House Committees on the Budget.

S. 320 – On January 29, 2015, Senator Elizabeth Warren (D-MA) introduced S. 320, the Medical Innovation Act. The bill would authorize the collection of supplemental payments to increase investments in medical research. S. 320 was referred to the Senate Committee on Health, Education, Labor and Pensions.

H.R. 596 – On February 3, 2015, the House passed by a vote of 239-186, H.R. 596, a bill to repeal the Patient Protection and Affordable Care Act (P.L. 111-148) and health care-related provisions in the Health Care and Education Reconciliation Act of 2010 (P.L. 111-152). The bill would task the House Committees on Education and the Workforce, Energy and Commerce, Judiciary, and Ways and Means to report legislation to the House of Representatives proposing changes to existing law within each committee's jurisdiction. Provisions of interest to NIH that would be repealed include the Patient Centered Outcomes Research Institute, the elevation of the National Institute on Minority Health and Health Disparities from a Center to an Institute, the establishment of an Interagency Pain Research Coordinating Committee, and provisions authorizing NIH to expand research on pain, congenital heart disease, and postpartum depression. The ACA also requires the Secretary of HHS to support emergency programs across Department and the Director of NIH to conduct research on new screening tests and methods for prevention and early detection of breast cancer in young women. The bill was introduced on January 28, 2015, by Representative Bradley Byrne (R-AL) and was jointly referred to the House Committees on Energy and Commerce, Education and the Workforce, Ways and Means, Judiciary, Natural Resources, Rules, House Administration, Appropriations, and Budget.

H.R. 744 – On February 4, 2015, Representative Chris Van Hollen (D-MD) introduced H.R. 744, the Medical Innovation Act. The bill, the companion to Senator Elizabeth Warren's S. 320, would authorize the collection of supplemental payments increase investments in medical research. H.R. 744 was referred to the House Committee on Energy and Commerce.

H.R. 777 – On February 5, 2015, Representative Kathy Castor (D-FL) introduced H.R. 777, the Permanent Investment in Health Research Act. The bill would amend the Public Health Service Act to provide funding for NIH. The bill was referred to the House Committee on Energy and Commerce, in addition to the Committees on the Budget and Appropriations.

H.R. 1468 – On March 19, 2015, Representative Chris Smith (R-NJ) introduced H.R. 1468, the Global Brain Health Act of 2015. The bill would galvanize United States Government programs in support of brain health for global victims of autism, hydrocephalus and Alzheimer's and other forms of dementia, and for other purposes. Title III includes provisions relevant to the NIA, which direct the Secretary of Health and Human Services to enter into negotiations with the World Health Organization to develop a global plan for addressing AD and other forms of dementia, to develop international partnerships to ensure cross-collaboration on this plan, and to work with other international partners to develop a Global Alzheimer's Disease and Dementia Fund, among other activities. The bill was referred to the House Committee on Energy and Commerce, in addition to the House Foreign Affairs Committee.

Other legislative items of interest:

At the request of Susan Ross, Clerk, House Appropriations Subcommittee on Labor, HHS, Education, NIH hosted a visit on January 20 for the new Chair of the Subcommittee, Representative Tom Cole (R-OK). The Chairman invited all of the members of the Subcommittee to join him and the attendees, in addition to the Chairman, were Representatives Steve Womack (R-AR), Dr. Andy Harris (R-MD), new member Charles Dent (R-PA), Rosa DeLauro (D-CT), and Nita Lowey (D-NY). Also attending were Susan Ross and John Bartrum from the Subcommittee; Stephen Steigleder, Minority Clerk; Sean Murphy, Maria Bowie, Steve Waskiewicz, and Stratton Edwards from Rep. Cole's office; Chris Meekins, Deputy Chief of Staff for Policy for Representative Harris and Irene Harris, daughter of the Congressman; Erik Anthony, LA for Representative DeLauro; and Dana Miller, Associate Appropriations staff for Representative Lowey.

On March 3, the House Appropriations Subcommittee, held a hearing on the FY2016 President's Budget for NIH. Francis Collins, Director, NIH, testified. He was accompanied by Anthony Fauci, Director, NIAID, Thomas Insel, Director, NIMH, Gary Gibbons, Director, NHLBI, Jon Lorsch, Director, NIGMS, and Nora Volkow, Director, NIDA.

On March 10, the Senate Committee on Health, Education, Labor, and Pensions held a hearing entitled "Continuing America's Leadership in Medical Innovation for Patients." Francis Collins, Director, NIH, and the Commissioner of FDA testified.

On March 25, the Senate Special Committee on Aging held a hearing on Alzheimer's Disease, entitled "The Fight Against Alzheimer's Disease: Are We on Track to a Treatment by 2025." Dr. Richard Hodes, Director, NIA, testified. Other witnesses included B Smith, former model, and restaurateur, who has been diagnosed with early-onset Alzheimer's disease, and her husband, Dan Gasby; Ronald Petersen, Ph.D., M.D, Professor of Neurology, Director and Chair, Cora Kanow Professor of Alzheimer's Disease Research, Mayo Clinic Alzheimer's Disease Research Center and Advisory Council on Alzheimer's Research, Care, and Services; Kimberly Stemley, Caregiver and Chief Financial Officer, Rx Outreach; and Heidi R. Weirman, M.D., Division Director of Geriatrics and Medical Director, Maine Medical Center and Elder Care Services, MaineHealth.

Submitted by: Melinda Kelley, Ph.D., Senior Health Policy Analyst, National Institute on Aging

STAFF CHANGES

Dr. Richard Suzman, director of NIA's Division of Behavioral and Social Research, passed away in the night of Wednesday, April 15. He was 72. As some of you may know, Richard had amyotrophic lateral sclerosis. His death is a deep loss for NIA and for the community at large.

Richard was one of the most creative and innovative scientists I know, who with an unrivaled energy and determination helped transform the behavioral and social sciences. He was a critical figure in advancing the science of demography and developed new fields, including the bio-demography of aging. In his 30 years of distinguished federal service, Richard led the development of several new transdisciplinary fields of study, including neuro-economics, social neuroscience, and behavioral genetics. His career changed our understanding of longevity and aging, integrating economic and social behavior with biological and clinical aspects of advancing age.

At NIH, his vision contributed to important trans-NIH initiatives. The Common Fund's interest in the Science of Behavior Change and Health Economics are already making a difference, through studies of new ways to intervene in health behaviors, including tobacco use, diabetes management, and the dissemination of and adherence to medical regimens. His understanding of how economics can affect health and aging has already changed trajectories for participation in pension savings in the U.S., for the benefit of today's older Americans and generations to come.

Perhaps his key achievement is the U.S. Health and Retirement Study, which has grown to encompass a group of connected international surveys that cover more than half the world's population. These related surveys allow researchers to compare data on aging cross-nationally, demonstrating how both common and unique biological, cultural, institutional, and policy features can impact health and well-being with age. The loss of Richard will not only be felt here, but internationally.

Richard was a tireless advocate for the best in science and for the health of older people and their families. We remember Richard Suzman, both the scientist and the irascible character, with admiration and affection. At a personal level, Richard was for me a constant example of what can be accomplished through vision, energy, and intellect. If I was ever tempted to lapse into complacency, Richard made it clear that this would not be tolerated.

Richard Hodes

Dr. Jyan-yu Austin Yang has joined the Division of Neuroscience as the Program Director for Etiology of Alzheimer's Disease in the Neurobiology of Aging Branch. He received his Ph.D. in Biological Sciences from the University of California, Irvine in 1993 and, following postdoctoral training in the cell biology of beta-amyloid at the same institution, Dr. Yang moved to New York University and its affiliate, the Nathan Kline Institute for Psychiatric Research, as an Assistant Professor. He moved back to the west coast in 2002 where he held faculty appointments in the Department of Pharmaceutical Sciences at the University of Southern California. Prior to joining the NIA, Austin was an Associate Professor in the Department of Anatomy and Neurobiology and in the Greenebaum Cancer Center at the University of Maryland School of Medicine. Dr. Yang's research over the years has centered on understanding the cellular and molecular events leading to Alzheimer's disease. He has focused on proteomic approaches, using new

mass spectrometry and bioinformatics techniques he developed, to define posttranslational modifications and degradation pathways of the tau and amyloid proteins that are involved in the pathogenesis of AD. In addition, his group has developed a series of computational tools for the analyses of various stable isotope-based shotgun proteomics datasets. Dr. Yang has served as an Ad Hoc reviewer for NIH, including NIA, study sections and was a regular member of the CSR Synapses, Cytoskeleton and Trafficking (SYN) study section.

While at NIA, Dr. Chen was responsible for oversight and development of the Sensory and Motor Disorders of Aging program in the Division. She brought application of cutting-edge technologies to the research enterprise through an initiative to encourage optogenetic approaches to aging brain research. Dr. Chen was an advocate for research on treatment and prevention of chronic pain in the elderly and served as the NIA liaison for the NIH Pain Consortium.

Carmen P. Moten, Ph.D., MPH., has joined the Scientific Review Branch, NIA, and as a Scientific Review Officer (SRO) she will deal mostly with applications on behavioral and social research. She comes from the Center to Reduce Cancer Health Disparities (CRCHD) at National Cancer Institute (NCI) where as a Program Director (PD), Dr. Moten planned, developed, and managed programs that addressed basic, clinical, and behavioral research designed to reduce and/or eliminate cancer and co-morbid health disparities. Prior to joining CRCHD, Dr. Moten served as PD of the Primary Care, Health Disparities, and Socio-Cultural Mental Health Services Research Programs in the Division of Services and Intervention Research at NIMH. There she provided scientific leadership and oversight of research and training grants, cooperative agreements, and FOAs. She collaborated with federal agencies, investigators, clinical practice groups and community organizations about research, training, and related activities that contribute to mental health treatment and health-related outcomes. Her work also included service on NIMH, NIH, HHS and inter-departmental committees addressing critical issues relevant to mental health and co-morbid translational research. Dr. Moten's research interests include behavioral epigenetics, psychobiology, epidemiology, health services research, health disparities, healthcare delivery, preventive interventions, social determinants of health community based participatory research, and other behavioral health related issues, such as, trauma, stigma, and risk and protective factors. She teaches a psychology course at Howard University where she has an appointment as an Adjunct Associate Professor.

Dr. Moten received her Ph.D. from Howard University, in Developmental and Personality Psychology and her MPH from the University of North at Chapel Hill, in Health Behavior and Health Education.

On February 6, 2015, Mr. Larry Pointer, Extramural Staff Assistant assigned to BSR by DEA, left NIA for a promotion at CSR.

On April 6, 2015, Ms. Anita Cherry joined NIA as an Extramural Staff Assistant assigned to BSR by DEA. Ms. Cherry is new to the Federal Government, but she has many years of experience in customer support, accounting, and managing special events and programs

INSTITUTE-SPONSORED MEETINGS, WORKSHOPS, and CONFERENCES

I. Past Meetings

GSIG SEMINARS (February 5 & May 7 & August 6, 2015)

This seminar series is sponsored by the trans-NIH GeroScience Interest Group (GSIG). The GeroScience Interest Group (GSIG) was formed to enhance opportunities for discussion of the intersection between the biology of aging and the biology of disease and conditions that are of interest across ICs. It is focused on basic biology, but with a longer view towards translation. These seminars will focus on the areas of aging and diverse aging-related diseases, with emphasis on the intersections between the basic biology of aging and the basic biology of the disease. Such topics are important to further the goals of the GSIG.
The three seminars are scheduled for Feb 5, 2015; May 7, 2015 and Aug 6, 2015.

(Contact(s): Drs. Felipe Sierra/Ronald Kohanski, DAB, 301/496-6402).

The Alzheimer's Disease Research Summit 2015: Path to Treatment and Prevention drew more than 500 leading researchers and advocates with a shared goal—to develop a scientific agenda that speeds the development of effective therapies to treat and prevent Alzheimer's disease (AD). Held Feb. 9-10 on the NIH campus and hosted by NIA, the conference focused on new research models and intensifying public-private collaborations to identify and speed the delivery of promising therapeutic targets
Learn more here: http://www.nia.nih.gov/research/agenda-alzheimers-disease-research-summit-2015 https://www.youtube.com/watch?v=ZAlGbzjO4oI . For more information, please contact Suzana Petanceska 301-496-9350, Email: petanceskas@nia.nih.gov.

Health Economics: Personalized Health Care and Prevention Steering Committee Meeting – February 25, 2015 - Bethesda, MD

The mandate for the Steering Committee (SC) for the cooperative agreements funded under RFA-RM-12-024 is to identify, develop, and implement strategies to realize value to the scientific community and the NIH beyond the contributions of the individual projects. The Steering Committee organized this meeting with researchers, officials from NIH and other agencies, guidelines-setting entities, health care providers, and insurers to identify needs and opportunities for economic research on personalization in health care. The report of the meeting is available on the Health Economics website. For additional information please contact Dr. John Haaga at BSR (301-496-3131).

NIA Sponsored Symposium on Aging at 56th Annual Drosophila Research Conference at Genetics Society of America (GSA) - March 6-7, 2015

Genetic model systems are very important for understanding the mechanisms of aging processes. For invertebrate models, the majority of aging research has been carried out in C. elegans. Compared to C. elegans, Drosophila has been under-utilized for aging research. Drosophila has many advantages over C. elegans, including more complex organ system, sophisticated behavior, and more distinctive aging phenotypes. The Drosophila Research Conferences, organized by Genetics Society of America, has been held every year for 55 years. We sponsored a session (symposium) on the topic of aging at this annual fly meeting. The objectives were: (1) to improve the representation of aging research at the meeting; (2) to showcase some NIA-funded research; (3) to attract fly researchers to the study of aging. The meeting was held on March 4-8, 2015 in Chicago, IL.

(Contact: Dr. Max Guo, DAB, 301/496-6402).

Subjective Well-being Measures in Interventional and Observational Studies in Older Individuals – March 12-13, 2015 – Bethesda, MD

The goals of this workshop were to identify measures of subjective well-being (SWB) that are most appropriate for use in observational and interventional studies in older individuals, and to provide investigators with the necessary knowledge and tools to successfully incorporate SWB measures into such studies. The meeting brought together select individuals with expertise in measurement of subjective well-being (SWB) and/or use of those measures in health-related studies, and individuals with expertise in observational and/or interventional research in older adults to encourage dialogue and cross-fertilization of ideas. This workshop was sponsored by the NIA Division of Behavioral and Social Research (DBSR) and the Division of Geriatrics and Clinical Gerontology (DGCG). The workshop generated recommendations that may lead to a publication as well as a future funding opportunity that, if approved for development, will be presented at a future NACA meeting.

Contact: Dr. Basil Eldadah, DGCG, 301-496-6761, or Dr. Lisbeth Nielsen, DBSR, 301-402-4156

Emotional and Health Consequences of Early Life Adversity: Preconference to the Society for Affective Science – April 9, 2015, Oakland, CA

The goal of this preconference workshop is to explore whether affective science can help to shed light on the mechanisms by which early life adversity affects physical health and well-being over the life course, and to potentially translate insights derived from this perspective into primary and secondary preventive interventions. This preconference workshop will bring together experts in: 1) the epidemiology of physical health consequences of early adversity; 2) the epidemiology of mental health consequences of early adversity; 3) how emotional development is altered by early adversity; 4) what the emotional characteristics of early adversity are in adulthood; 5) what is known about central and peripheral physiological mechanisms of 1 and 2; and 6) how affective science can inform clinical interventions to improve health outcomes in those exposed to early life adversity. For additional information please contact Dr. Lis Nielsen at BSR (301-402-4156).

NIA Sponsored Symposium on Aging at 2nd Puerto Rico Cell Signaling Meeting - April 10, 2015

This one day meeting, organized by graduate students and postdoctoral fellows, presents current research in cell signaling and promotes collaborations among scientists. This meeting is open to basic and clinical investigators, graduate and undergraduate students currently working in the field of cell signaling. This year's scientific theme is on aging. The topics of presentations include "epigenetic based changes in mesenchymal stem cell (MSC) function with aging", "the rhesus monkey as a model of translational research age-related disease", and "impact of aging on nutrient-induced signaling pathways in mesenchymal stem cells". The objective is to promote aging research and attract young scientists, including students and postdocs, from diverse backgrounds into aging research.

(Contact: Dr. Max Guo, DAB, 301/496-6402).

Developing Biomarker Arrays Predicting Sleep and Circadian-Coupled Risks to Health April 27-28, 2015 - Bethesda, MD

NIA, along with NHLBI and the Sleep Research Society, will co-sponsor a workshop entitled "Developing Biomarker Arrays Predicting Sleep and Circadian-Coupled Risks to Health" on April 27-28, 2015 in Bethesda, MD. The goal of this workshop is to discuss research needed to develop diagnostic tools to facilitate the assessment of health risks associated with sleep/circadian deficiency and whether these health risks are reduced by treatment. The workshop will bring together prominent researchers with expertise in biomarkers and sleep in equal proportions. Ample time is planned for in person small group discussions so that experts in biomarker development can explore potential avenues with experts in sleep and circadian biology. Four "use cases" have been identified to focus the discussion of biomarker development: a) acute sleep loss, b) chronic insufficient sleep, c) circadian phase and circadian disruption, and d) the common disorder obstructive sleep apnea. Workshop recommendations will be used to inform NIH, CDC, and other Federal Agencies concerned with the risks that sleep deprivation poses to health, public safety, and performance metrics. For more information please contact Miroslaw (Mack) Mackiewicz (DN) 301-496-9350, Email: mackiewiczm2@mail.nih.gov.

NIA Sponsored Symposium "Rejuvenating the Aging Immune System" at the American Association of Immunologists (AAI) Annual Meeting - May 9, 2015

This NIA sponsored symposium is due to be held at the American Association of Immunologists annual meeting on May 9, 2015 in New Orleans. LA. The NIA sponsors a symposium each year to highlight recent findings in the area of Rejuvenating the Aging Immune System.

The purpose of this symposium is to have speakers present state of the science findings on this research topic.

(Contact: Dr. Rebecca Fuldner, DAB, 301/496-6402).

II. Future Meetings

NAS Board on Behavioral, Cognitive, and Sensory Sciences Spring Meeting: Developing Interventions to Reduce Social Isolation and/or Loneliness in Mid- to Late-Life – June 4, 2015 - Washington DC

Purpose and Objectives:

BSR has been advised in the course of its quadrennial divisional review by the National Advisory Council on Aging to expand our interventions portfolio in this area. We seek expert input on the most promising strategies for advancing intervention efforts in this area.

Questions for an Expert Meeting:

- What study designs will permit rigorous testing of theory; e.g., shedding light on pathways linking social contexts and individual differences to loneliness and/or social isolation, or explicitly testing theories about how to change social relationships?

- What strategy holds greatest promise at this juncture? Should one focus on small studies with shorter term outcomes, targeting social isolation, loneliness, and networks rather than health to demonstrate ability to impact these targets? Should one conduct

larger scale trials to permit identification of responders and non-responders, and the mechanisms that account for response effects?

For additional information please contact Dr. Lis Nielsen at BSR (301-402-4156).

NAS Committee on Population Spring Meeting: Future Directions in the Demography of Aging – June 2015 - Washington DC

As part of its regular semi-annual meeting, the Committee on Population will bring together small group of experts to discuss future directions in the demography of aging.

For additional information please contact Dr. John Haaga at BSR (301-496-3131).

NAS Board on Behavioral, Cognitive, and Sensory Sciences Meeting on Understanding Pathways to Healthy Aging – June 11-12, 2015 - Washington DC

The NACA 2013 BSR Review recommended the measurement of time-use and physical activities in population surveys to support aging research in a number of domains. Specifically, they noted that detailed information on the context of behavior can inform more effective interventions and that the collection of activity, biomarker, and time use data would support research that illuminates the pathways by which social, psychological, economic, and behavioral factors affect health in middle-aged and older adults. BSR will engage the experts at the Committee on National Statistics on the subject of time-use and activity measurement in surveys to begin developing plans to address the NACA recommendation.

For additional information please contact Dr. Lis Nielsen at BSR (301-402-4156.)

Ninth Annual Division of Aging Biology New Investigators Forum (DAB NIF) - June 18-19, 2015

Purpose: Outreach

The purpose of the forum is to bring together new awardees (i.e. Principal Investigators who can be identified as "new investigators") in the spring of the year following their award, in order to allow NIA program staff to get acquainted with new PIs as well as allow the participants to network with each other. Each new PI will give a brief talk describing the planned research (or results to date) *with an emphasis on how it relates to the area of aging research.* The overriding goal of the meeting is to encourage continued success for the new PIs as well as attempt to maintain their focus on the area of aging research. As a result of past meetings we have found that the PIs have indeed set up new collaborations. They also are much more likely to keep us informed of their new publications and progress.

The meeting will start with a keynote address by an eminent aging researcher (Dr. Steven Austad).

We propose a workshop to be held on June 18-19, 2015 in Bethesda, MD.

(Contact: Dr. Nancy Nadon, DAB, 301/496-6402).

Sleep in Alzheimer's Disease: Molecules, Networks, People

Alzheimer's Association International Conference 2015 July 18-23, 2015 - Washington, DC

The National Institute on Aging will cosponsor a Featured Research Session entitled "Sleep in Alzheimer's Disease: Molecules, Networks, People" during the 2015 Alzheimer's Association International Conference (AAIC), July 18-23, 2015 in Washington, D.C. Older adults with AD often exhibit sleep disturbances and circadian clock disruptions. Although this has been interpreted as a consequence of AD, there is evidence that sleep disturbances may contribute to the risk of Alzheimer's disease. Preclinical signs of AD are associated with poor sleep quality, Abeta (A□□ accumulation in the brain predicts and exacerbates sleep disruption in humans and in animal models, and experimental manipulations to increase sleep result in decreases in Aβ deposition. Although mechanisms underlying the link between sleep and AD are not clear, studies suggest that synaptic activity driven A□ release is lower during sleep and that the clearance of Aβ from the brain through the glymphatic pathway is facilitated by sleep through an increase in the volume of interstitial space. Functionally, this interaction may offer a novel pathway through which Aβ leads to hippocampal memory dysfunction by impairing sleep-dependent memory consolidation, thus contributing to age-related cognitive decline. Effective interventions exist to improve sleep and these could be utilized in AD prevention. The goals for this session are to (1) describe the relationship between disordered sleep, cognitive decline, and AD, (2) discuss mechanisms by which sleep disturbances might lead to AD-related pathologies, and (3) explore sleep interventions that could be tested in the human population to augment cognitive health. For more information please contact Miroslaw (Mack) Mackiewicz (DN) 301-496-9350, Email: mackiewiczm2@mail.nih.gov.

Renal Pathophysiology - July 20, 2015

Over the years, NIA has supported renal research (both basic science and clinical aspects) that is applicable to issues that we deal with in the elderly. Although we continue to see interests on renal pathophysiology from the research community, we have lost many senior researchers, who had support from NIA.

However, there are significant scientific advances in several areas that are highly relevant to aging and the geriatric population. These areas include animal models, renal biomarkers in acute and chronic kidney disease (CKD, renal fibrosis, autophagy, proteostasis and others). Even though nephrology researchers have begun to apply these advances, they are still not fully exploited by the community. In addition, technologies such as proteomics and metabolomics and their utility to understand renal pathophysiology could be part of this workshop.

We propose an exploratory workshop to be held on July 20, 2015 in Bethesda, MD.

(Contact: Dr. Mahadev Murthy, DAB, 301/496-6402).

Metrics for the Rate of AGING - Summer, 2015

Metrics for the rate of aging can be useful in several contexts, but the primary value is to evaluate human health as we age. If health is good we can anticipate more active life, less disability, less disease and lower health care costs. If health is poor, we anticipate the converse for each of these. The "rate of aging" should be informative of improving, steady or declining health over time. To make such assessments requires some metrics to describe the rate of

aging quantitatively. These metrics can also be used to determine whether interventions are effective in 'slowing' this rate of aging.

The objective of this workshop will be to evaluate potential metrics for the rate of aging. An initial assessment suggests the following six areas should be considered in this workshop, where these can be clustered in three groups by their similarities: *X.* Multiple Chronic Conditions, Multiple Chronic Diseases; *Y.* Frailty, Resilience; *Z.* Allostatic Load, Molecular Markers. Using these three groups, is it possible to define three axes for metrics that together reveal a rate of aging, but which also can define a "health space" for adults.

Some specific discussions would be appropriate. In Group X: Evaluate the independence or inter-relatedness of chronic conditions and diseases. In Group Y: Evaluate the predictive value of frailty and resilience (and in the case of resilience, what parameters would be appropriate measures, since this may not be sufficiently well-defined). In Group Z: Evaluate the diagnostic versus predictive value for health of parameters at the molecular level.

An exploratory workshop will be held in Summer, 2015 in Bethesda, MD.

(Contact: Dr. Ronald Kohanski, DAB, 301/496-6402).

Assessment of Resilience in Clinical Population - Summer, 2015

The concept of physiological resilience was originally discussed in a workshop convened by DAB in August 2014. The focus of DAB's meeting was on the development of measures of resilience which could be used in intervention testing studies in rodent models. DGCG's proposed meeting is intended as a follow up and will focus on the application of the physiological resilience concept in humans. DGCG is proposing a workshop (a day and a half) to discuss the conceptual basis of resilience, how to operationalize resilience, including the methodological issues/challenges of assessing resilience at different ages and in different clinical settings and research designs (e.g., observational vs. interventional studies). DAB has agreed to co-sponsor this meeting if funds are available.

We propose an exploratory workshop to be held in Summer, 2015 in Bethesda, MD.

(Contact(s): Dr. Felipe Sierra, DAB, 301/496-6402, Dr. Evan Hadley, DGCG, 301/496-6761).

Biology of the Genes and Pathways Important for Aging AND Longevity in Humans - Summer, 2015

Many genes and pathways have now been identified to be associated with aging and longevity. For example, FOXO3A, has been shown to be associated with longevity in more than 11 studies in different ethnic human populations. There are overwhelming interests in the underlying mechanisms and translation of these discoveries. However, the functions of these genes and their genetic variants in humans still remain largely obscure. This workshop will evaluate the status of the research on these genes and their genetic variants, and discuss future research directions on understanding the biology and physiology of these genes and their genetic variants in order to translate these discoveries into benefits for human health.

We propose an exploratory workshop to be held in Summer, 2015 in Bethesda, MD.

(Contact: Dr. Max Guo, DAB, 301/496-6402).

GENERAL INFORMATION/STAFF AWARDS

On March 27, 2015, the Women Scientist Advisors (WSA) held a special program in conjunction with the National Institute on Drug Abuse (NIDA) to honor the WSA Achievement Awardees. Simonetta Camandola, Ph.D., Laboratory of Neurosciences, received the NIA Staff Scientist Award and Jennifer Illuzzi, Ph.D., Laboratory of Molecular Gerontology received the NIA Fellow Award.

Dr. Kevin Volpp has been selected to share the 8th Matilda White Riley Award and Lecture in Behavioral and Social Sciences with Dr. Jeanne Brooks-Gunn. The Lecture will be a central feature of the NIH Office of Behavioral and Social Research (OBSSR) 20th Anniversary celebration on June 23, 2015. The Matilda White Riley Award was established by OBSSR to honor the memory of Matilda White Riley (1911-2004) who was the Associate Director for Behavioral and Social Research at the NIA and who also served as a senior NIH spokesperson on the behavioral and social sciences at NIH.

Publications & Online Resources

National Research Council and Institute of Medicine. (2015). Measuring the Risks and Causes of Premature Death: Summary of Workshops. H.G. Rhodes, Rapporteur. Committee on Population, Division of Behavioral and Social Sciences and Education. Board on Health Care Services, Institute of Medicine. Washington, DC: The National Academies Press.
This report summarizes the proceedings of two workshops convened in September 2013 and September 2014 to consider issues in the measurement of the risks and causes of premature death. The workshops were sponsored by NIA and convened by the Committee on Population. The workshops were organized by a seven-member steering committee composed of experts in the fields of demography, population health, epidemiology, and health measurement. The committee was co-chaired by Linda Waite of the University of Chicago in 2013, and Eileen Crimmins of the University of Southern California in 2014. The committee provided guidance in developing the workshop agendas, securing expert presentations, and facilitating the conduct of the workshops. The committee also benefited from the input of Richard Suzman, then director of the NIA Division of Behavioral and Social Research, prior to and during the two workshops.

Certain behaviors, exposures and predispositions place people at risk for early death or poor health outcomes. The impetus for the workshops was to better understand the risk factors most amenable to prevention and health policy efforts, primarily behavioral risk factors. The definition of "early" can vary. Michael McGinnis' initial work focused on deaths prior to age 75, but later work has focused on deaths before age 80. The WHO Global Burden of Disease compares years of life lost against a reference age of 86, or the highest average lifespan of a country with a population over 5 million. Other studies have focused on survival to age 70. This document focuses, among other things, on implications of these definitions, sources of data, and other methodological considerations.

OCPL Contribution to the May 2015 Director's Status Report

Publications and Online Resources

Books and Fact Sheets:

- Ejercicio y actividad física: su guía diaria del Instituto Nacional Sobre el Envejecimiento (updated and reprinted)
- Workout to Go: A Sample Exercise Routine from the National Institute on Aging at NIH (reprinted)
- AgePage: Healthy Eating After 50 (reprinted)

E-newsletters:

- Connections (Spring 2015)

Web products/content (new):

- Early-Onset Alzheimer's Disease: A Resource List
- AMP-AD web pages
  - Accelerating Medicines Partnership-Alzheimer's Disease (AMP-AD)
  - AMP-AD Biomarkers Project AMP-AD Target Discovery and Preclinical Validation Project
- Alzheimer's disease research recruitment pages
  - Volunteer for Alzheimer's Research
  - Spread the Word About Volunteering
- Alzheimer's and dementia resources for professionals
- NIHSeniorHealth added a new topic on skin care and aging

(For more information about NIA's publications and online resources, contact Vicky Cahan, Director, OCPL, Ph. 301-496-1752.)

Media & Outreach

Press releases

- NIH-led effort launches Big Data portal for Alzheimer's drug discovery
- Hypothermia: A Cold Weather Hazard

Social Media

- @NIAGo4Life Twitter has 4,000+ followers with an additional 2,500+ subscribing to daily e-alert of tweets
- @Alzheimers_NIH Twitter has 2,800+ followers with more than 3,650 subscribing to daily e-alert of tweets
- "Inside NIA: Blog for Researchers" has11,600+ subscribers and continues to spur active online conversations
- NIHSeniorHealth's weekly Healthy Aging tips has 35,000+ subscribers
- NIA's YouTube channel now features 112 videos, including a new video about the recent AD Summit

Meetings & Exhibits

- American Society on Aging meeting, Chicago, IL, March 23-25 -- OCPL staff presents on syndicating website content and research recruitment
- In February, Drs. Richard Hodes and Marie Bernard met with University of Illinois at Urbana-Champaign Chancellor, Dr. Phyllis Wise, to discuss the launch of their new medical school.

- In February, Drs. Richard Hodes, Neil Buckholtz, and other senior staff met with representatives of the American Neurological Association.
- In February, Drs. Richard Hodes, Marie Bernard, and other senior staff met with the Friends of the NIA coalition.
- In March, Drs. Richard Hodes, Marie Bernard, and other senior staff met with the Ad Hoc Group for Medical Research.
- In March, Dr. Marie Bernard and other senior staff met with representatives of NEOMED (Northeast Ohio Medical University).
- In March, Drs. Richard Hodes, Marie Bernard, and other senior staff met with representatives of the American Geriatrics Society.

(For more information about NIA's conferences or exhibits, contact Vicky Cahan, Director, OCPL, Ph. 301-496-1752. For more information about NIA's professional meetings, contact Dr. Melinda Kelley, Legislative Officer, Ph. 301-451-8835.)

NEW NOTICES AND INITIATIVES RELEVANT TO THE NATIONAL INSTITUTE ON AGING (NIA) For the JANUARY 2015 Council Meeting

For 'Notices' and 'Research Initiatives' with NIA's participation or interest please visit these two websites: http://www.nia.nih.gov/research/funding and http://www.nia.nih.gov/research/dea/nih-funding-policies (Please look for 'Recent Changes in NIH Policy' on this web link).